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## **CLAIMS**

What is claimed is:

1. An immunomodulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the formula:

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5'-X<sub>1</sub> X<sub>2</sub> A X<sub>3</sub> C G X<sub>4</sub> T C G-3' (SEQ ID NO: 62)
wherein X<sub>1</sub> is T, G, C or Z, wherein Z is 5-bromocytosine;
wherein X<sub>2</sub> is T, G, A or U;
wherein X<sub>3</sub> is T, A or C;
wherein X<sub>4</sub> is T, G or U; and
wherein the ISS is not 5'-TGAACGTTCG-3' (SEQ ID NO: 63) or 5'-GGAACGTTCG-3' (SEQ ID NO: 64).
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- 2. An immunomodulatory polynucleotide according to claim 1, wherein the ISS is selected from the group consisting of TGAACGUTCG (SEQ ID NO: 67), TGACCGTTCG (SEQ ID NO: 68), TGATCGGTCG (SEQ ID NO: 69), TGATCGTTCG (SEQ ID NO: 70), TGAACGGTCG (SEQ ID NO: 71), GTAACGTTCG (SEQ ID NO: 72), GTATCGGTCG (SEQ ID NO: 73), GTACCGTTCG (SEQ ID NO: 74), GAACCGTTCG (SEQ ID NO: 75), ZGACCGTTCG (SEQ ID NO: 76), wherein Z is 5-bromocytosine, CGAACGTTCG (SEQ ID NO: 77), CGACCGTTCG (SEQ ID NO: 78), ZGAACGTTCG (SEQ ID NO: 79), wherein Z is 5-bromocytosine, TTAACGUTCG (SEQ ID NO: 82), TUAACGUTCG (SEQ ID NO: 81) and TTAACGTTCG (SEQ ID NO: 80).
- 3. An immunomodulatory polynucleotide according to claim 2, wherein the ISS is selected from the group consisting of TGAACGUTCG (SEQ ID NO: 67), GAACCGTTCG (SEQ ID NO: 75) and CGAACGTTCG (SEQ ID NO: 77).

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5-bromocytosine.

- 4. An immunomodulatory polynucleotide according to claim 3 comprising a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 18, SEQ ID NO: 19 and SEQ ID NO: 132.
- 5. An immunomodulatory polynucleotide comprising an immunostimulatory sequence (ISS), wherein the ISS comprises the formula:

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5'-X<sub>1</sub> X<sub>2</sub> A X<sub>3</sub> Z G X<sub>4</sub> T C G-3' (SEQ ID NO: 65)
wherein Z is 5-bromocytosine;
wherein X<sub>1</sub> is T, G, C or Z, wherein Z is 5-bromocytosine;
wherein X<sub>2</sub> is T, G, A or U;
wherein X<sub>3</sub> is T, A or C;
wherein X<sub>4</sub> is T, G or U; and
wherein the ISS is not 5'-TGAAZGTTCG-3' (SEQ ID NO: 66), wherein Z is
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6. An immunomodulatory polynucleotide according to claim 5, wherein the ISS is selected from the group consisting of TGAAZGUTCG, (SEQ ID NO: 83) TGACZGTTCG (SEQ ID NO: 84), TGATZGGTCG (SEQ ID NO: 85), GTATZGGTCG (SEQ ID NO: 86), GTACZGTTCG (SEQ ID NO: 87), GAACZGTTCG (SEQ ID NO: 88), GAAAZGUTCG (SEQ ID NO: 89), ZGACZGTTCG (SEQ ID NO: 90), CGAAZGTTCG (SEQ ID NO: 91), ZGAAZGTTCG (SEQ ID NO: 92), ZGAAZGUTCG (SEQ ID NO: 93), TTAAZGUTCG (SEQ ID NO: 94), TUAAZGUTCG (SEQ ID NO: 95) and TTAAZGTTCG (SEQ ID NO: 96), wherein Z is 5-bromocytosine.

7. An immunomodulatory polynucleotide according to claim 6, wherein the ISS is selected from the group consisting of ZGAAZGUTCG (SEQ ID NO: 93) and GAAAZGUTCG (SEQ ID NO: 89), wherein Z is 5-bromocytosine.

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- 8. An immunomodulatory polynucleotide according to claim 7 comprising a sequence selected from the group consisting of SEQ ID NO: 35 and SEQ ID NO: 36.
- 9. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide further comprises at least one TCG sequence.
- 10. An immunomodulatory polynucleotide according to claim 9, wherein the TCG sequence is adjacent to the 5' end of the ISS.
- 11. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide further comprises a TCGA sequence.
- 12. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide further comprises at least one T, 5-bromocytosine, G sequence.
- 13. An immunomodulatory polynucleotide according to claim 12, wherein the T, 5-bromocytosine, G sequence is adjacent to the 5' end of the ISS.
- 14. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide further comprises a T, 5-bromocytosine, G, A sequence.
- 15. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is less than about 150 bases or base pairs in length.

16. An immunomodulatory polynucleotide according to claim 1 or claim 5,
wherein the immunomodulatory polynucleotide is less than about 100 bases or base
pairs in length.
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17. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is less than about 50 bases or base pairs in length.

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18. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is single-stranded.

19. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is double-stranded.

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20. An immunomodulatory polynucleotide according to claim 1 or claim 5, wherein the immunomodulatory polynucleotide is stabilized.

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21. An immunomodulatory polynucleotide according to claim 20, wherein the polynucleotide comprises a phosphorothioate bond.

22. An immunomodulatory composition comprising an immunomodulatory polynucleotide according to claim 1 or claim 5.

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23. An immunomodulatory composition according to claim 22 further comprising a pharmaceutically acceptable excipient.

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- 24. An immunomodulatory composition according to claim 22 further comprising an antigen.
- 25. An immunomodulatory composition according to claim 24 further comprising a pharmaceutically acceptable excipient.
  - 26. An immunomodulatory polynucleotide/microcarrier (IMP/MC) complex, comprising:
  - a polynucleotide according to claim 1 linked to a biodegradable microcarrier (MC), wherein said MC is less than 10  $\mu$ m in size.
  - 27. An immunomodulatory polynucleotide/microcarrier (IMP/MC) complex, comprising:
  - a polynucleotide according to claim 5 linked to a biodegradable microcarrier (MC), wherein said MC is less than 10  $\mu$ m in size.
  - 28. A method of modulating an immune response in an individual comprising administering to an individual an immunomodulatory polynucleotide according to claim 1 or claim 5 in an amount sufficient to modulate an immune response in said individual.
  - 29. The method of claim 28, wherein said individual suffers from a disorder associated with a Th2-type immune response.
- 25 30. The method of claim 29, wherein said disorder associated with a Th2-type immune response is an allergy or asthma.

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- 31. The method of claim 28, wherein said individual has an infectious disease.
- 32. A method of increasing interferon-gamma (IFN- $\gamma$ ) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 1 or claim 5 to said individual in an amount sufficient to increase IFN- $\gamma$  in said individual.

- 33. The method of claim 32, wherein said individual has idiopathic pulmonary fibrosis.
- 34. A method of increasing interferon-alpha (IFN- $\alpha$ ) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 1 or claim 5 to said individual in an amount sufficient to increase IFN- $\alpha$  in said individual.

- 35. The method of claim 34, wherein said individual has a viral infection.
- 20 36. A method of increasing interferon-alpha (IFN- $\alpha$ ) in an individual, comprising:

administering an immunomodulatory polynucleotide according to claim 9 to said individual in an amount sufficient to increase IFN- $\alpha$  in said individual.

- 37. The method of claim 35, wherein said individual has a viral infection.
- 38. A method of increasing interferon-alpha (IFN- $\alpha$ ) in an individual, comprising:

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administering an immunomodulatory polynucleotide according to claim 11 to said individual in an amount sufficient to increase IFN- $\alpha$  in said individual.

- 39. The method of claim 38, wherein said individual has a viral infection.
- 40. A method of ameliorating a symptom of an infectious disease in an individual, comprising:

administering an effective amount of an immunomodulatory polynucleotide according to claim 1 or claim 5 to the individual, wherein an effective amount is an amount sufficient to ameliorate a symptom of said infectious disease.

- 41. The method of claim 40, wherein said infectious disease is an infectious disease caused by a cellular pathogen.
- 42. The method of claim 41, wherein said infectious disease caused by a cellular pathogen is selected from the group consisting of mycobacterial disease, malaria, leishmaniasis, toxoplasmosis, schistosomiasis and clonorchiasis.
- 43. A method of ameliorating a symptom of an IgE-related disorder in an individual, comprising:

administering an effective amount of an immunomodulatory polynucleotide according to claim 1 or claim 5 to an individual having an IgE-related disorder, wherein an effective amount is an amount sufficient to ameliorate a symptom of said IgE-related disorder.

44. The method of claim 43, wherein said IgE-related disorder is allergy.

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- 45. The method of claim 43, wherein said IgE-related disorder is an allergy-related disorder.
  - 46. The method of claim 43, wherein said IgE-related disorder is asthma.
- 47. A kit comprising an immunomodulatory polynucleotide according to claim 1 or claim 5.
- 48. The kit of claim 47, further comprising instructions for use of the immunomodulatory polynucleotide for immunodulation of an individual.